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A randomized clinical trial of postoperative adjuvant therapy for elderly breast cancer patients: Conditions of obtaining informed consent and reasons for declining participation

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Background

- The National Surgical Adjuvant Study of Breast Cancer 07 (N-SAS BC 07) is a randomized clinical trial (RCT) in women over 70 years with HER2-positive primary breast cancer (Sawaki M, et al. Jpn J Clin Oncol 2011;41:709-12).
- There are few RCTs examining adjuvant treatment in elderly breast cancer patients.
- While obtaining informed consent is essential for participation in clinical studies, there is little information on the frequency of agreement to participate among elderly patients.
- Furthermore, elderly patients might have specific reasons to decline participation.
- There have been no previous RCTs in elderly breast cancer patients, and it was not possible to predict the number of patients who would agree to participate when N-SAS BC 07 was planned. In order to comprehensively assess the effect of postoperative adjuvant therapy in elderly breast cancer patients, we prospectively evaluated the reasons why eligible patients declined to participate.

Objective

1. To examine the obtainment of informed consent for N-SAS BC 07-RCT and the reasons for declining participation
2. To investigate what clinicopathological backgrounds influenced elderly patients to participate this RCT

Materials & Methods

- The primary aim of the N-SAS BC 07 was to investigate the benefit of trastuzumab monotherapy compared with the combination of trastuzumab and chemotherapy.
- Key inclusion criteria were as follows
  - women between 70 and 80 years old with HER2-positive breast cancer
  - women who received curative operation
  - stage I to IIIA with sufficient organ function
- In N-SAS BC 07 trial, patients were randomized to receive either trastuzumab plus chemotherapy or trastuzumab monotherapy (07-RCT group).
- A cohort study (07-Cohort group) was planned for patients who did not assign informed consent. The patients were also registered in a cohort study to prospectively evaluate the subsequent treatment options and prognosis (07-Cohort) (Fig. 1). In 07-Cohort study, patients were treated with Investigator's choice.
- This study examined the obtainment of informed consent for N-SAS BC 07-RCT and the reasons for declining participation in the RCT at registration, and compared the clinicopathological backgrounds between 07-RCT group and 07-Cohort groups.

Results

- 398 eligible patients have been recruited.
- We show the patient's characteristics (Table 1).
- Informed consent to participate in N-SAS BC 07 has been obtained from 275 patients (69%) and 123 patients (31%) who declined to participate in the RCT have been registered in the 07-Cohort.
- The common reasons to decline participation in the RCT are shown in Fig. 2.
- The common reasons to decline participation in the RCT were "cannot choose the treatment option (55.1%)", "refused chemotherapy (20.3%)", "wanted chemotherapy (9.3%)", "anxious about participating in the clinical trial (9.3%)" and "family opposition (7.6%)".
- The mean ages of the patients in N-SAS BC 07-RCT and 07-Cohort at entry were 73.9 and 74.6 years old, respectively.
- There were no differences in stage, surgical procedure, lymph node metastasis, or co-morbidities (hypertension, diabetes mellitus, osteoporosis, hyperlipidemia) between two groups.
- The estrogen receptor (ER) positive rate in 07-RCT and 07-Cohort groups was 37.0% and 52.5%, respectively, which indicated that the ER positive rate was higher in 07-Cohort group (p=0.01, χ^2 test).

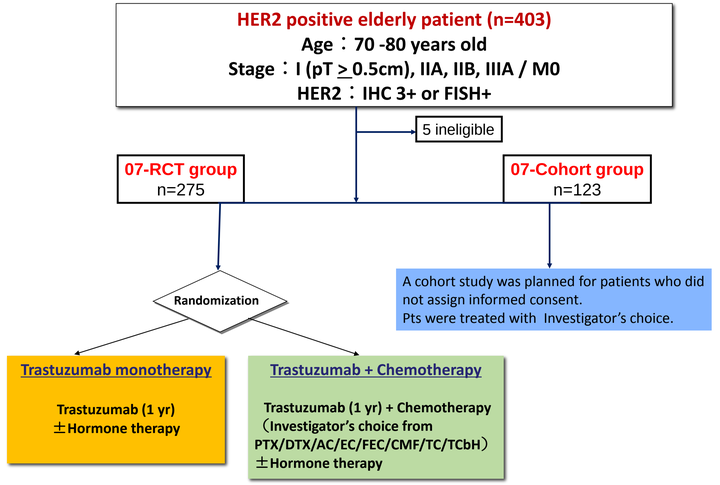

Fig.1. Study Consort
Registration Trial Number: NCT01104935 , UMIN000002349

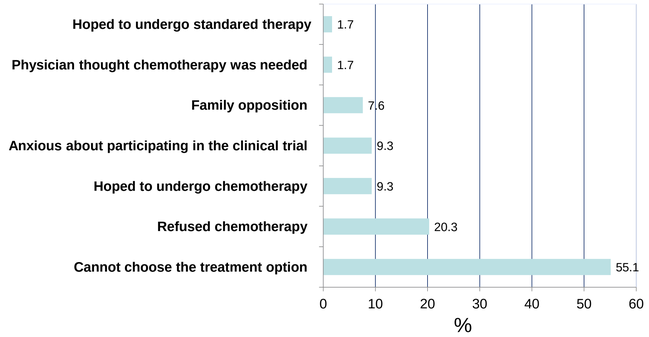

Fig. 2. The Reason to Decline Participation in the RCT (n=118)

Table 1. Patient's Characteristics

		07-RCT group (n= 262) n (%)	07-Cohort group (n=118) n (%)	*p*-value
Stage	I	109 (42.3)	50 (42.4)	0.72
	IIA	112 (43.4)	49 (41.5)	
	IIB	33 (12.8)	15 (12.7)	
	IIIA	4 (1.6)	4 (3.4)	
Surgery	Mastectomy	183 (69.8)	81 (68.7)	0.89
	Partial mastectomy	77 (29.4)	36 (30.5)	
	Others	2 (0.8)	1 (0.8)	
Surgical marjin	>5mm	62 (80.5)	25 (69.4)	0.4
	≤5mm	15 (19.5)	11 (30.6)	
Lymph node metastasis	Negative	203 (77.5)	81 (68.6)	0.07
	Positive	59 (22.5)	37 (31.4)	
Number of lymph node metastasis	0	203 (77.5)	81 (68.6)	0.14
	1	35 (13.4)	22 (18.6)	
	2	14 (5.3)	12 (10.2)	
	3	10 (3.8)	3 (2.5)	
Pathology	Invasive ductal carcinoma	243 (92.8)	110 (93.2)	0.49
	Invasive lobular carcinoma	9 (3.4)	2 (1.7)	
	Special type	10 (3.8)	6 (5.1)	
Estrogen Receptor	Negative	148 (56.5)	52 (44.1)	**0.01**
	Equivocal	17 (6.5)	4 (3.4)	
	Positive	97 (37.0)	62 (52.5)	
Progesteron Receptor	Negative	181 (69.1)	78 (66.1)	0.72
	Equivocal	22 (8.4)	9 (7.6)	
	Positive	59 (22.5)	31 (26.3)	
Major Comorbidity				
Hypertension	No	148 (56.5)	73 (61.9)	0.33
	Yes	114 (43.5)	45 (38.1)	
Diabetes	No	227 (86.6)	104 (88.1)	0.68
	Yes	35 (13.4)	14 (11.9)	
Osteoporosis	No	235 (89.7)	106 (89.8)	0.97
	Yes	27 (10.3)	12 (10.2)	
Hyperlipidemia	No	195 (74.4)	93 (78.8)	0.36
	Yes	67 (25.6)	25 (21.2)	
Others	No	204 (77.9)	91 (77.1)	0.87
	Yes	58 (22.1)	27 (22.9)	

Summary

- Since N-SAS BC 07 investigated whether elderly patients with HER2-positive breast cancer should undergo chemotherapy, we expected the rate of consent for registration to be small. However, almost 70% of the patients accepted informed consent.
- The most common reason to decline participation in N-SAS BC 07-RCT was "cannot choose the treatment option" and the majority refused chemotherapy.
- ER-positivity was higher in the 07-Cohort group, which suggested that ER expression in the patients with HER2-positive breast cancer might influence their decision to participate in the study or to choose the treatment option.

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